

# Thermal Cyclization of Nonconjugated Aryl–Yne–Carbodiimide Furnishing a Dibenzonaphthyridine Derivative

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**The reagent-free C<sup>2</sup>–C<sup>7</sup> thermal cyclization of a nonconjugated aryl–yne–carbodiimide yielded a dibenzo-[b,g][1,8]naphthyridine derivative, whose congeners are known to possess fascinating pharmacological properties. This is the first heteroaromatic compound prepared by the thermal cycloaromatization of “nonconjugated” aryl–ynes.**

**Key words** nonconjugated; aryl–yne carbodiimide; dibenzonaphthyridine; thermal cyclization; C<sup>2</sup>–C<sup>7</sup>

Conjugated enyne compounds have received considerable attention in the broad field of chemistry, because of their unique cyclization reactions affording aromatized products by way of radical intermediates capable of DNA cleavage.<sup>2–8)</sup> To date, a number of polyenyne compounds, including both natural<sup>2,4,7)</sup> and artificial products,<sup>3,7,8)</sup> have been synthesized to evaluate their reactivity and to develop more potent and selective antitumor agents, however, modification of the conjugated enyne core structures has not been well investigated. We focused on nonconjugated polyenyne systems and found that nonconjugated aryl–ynes and aryl–yne–allenes undergo thermal cycloaromatization (CA) reactions<sup>9–14)</sup> while cleaving DNA.<sup>15–17)</sup> Thus, as a next goal, we set a reagent-free thermal isomerization of nonconjugated aryl–yne systems, which involves homolyses of carbon–nitrogen (C–N) unsaturated bonds to afford useful azaaromatic compounds *via* a domino radical reaction.<sup>18)</sup>

As target polycyclic aromatic compounds, we focused on dibenzonaphthyridine derivatives, which have never been synthesized *via* thermal isomerization of aryl–ynes, despite their fascinating and intriguing pharmacological properties.<sup>19–23)</sup> In order to provide a novel synthetic methodology of dibenzonaphthyridines, we planned to examine the CA reactions of nonconjugated aryl–yne–carbodiimides (AYCs). Carbodiimide is considered to be an aza-equivalent of allene, and more importantly, canceled dipole moments of C–N bonds are expected to facilitate the homolytic cleavage of the C–N bond to form radical species. The Wang<sup>24–28)</sup> and the Schmittel<sup>29–31)</sup> groups have recently reported the thermal CA of AYCs, but their scopes are limited to conjugated systems, whose electronic and steric environments are far different from nonconjugated ones, and which would be unable to provide dibenzonaphthyridine derivatives. Herein, we report the synthesis and the CA reactions of AYCs **1** and **2**.

As AYC substrates, we selected two compounds (Fig. 1). One possesses a conjugated aryl–yne and a dependent carbodiimide moiety (**1**) and the other is equipped with a conjugated aryl–carbodiimide and a dependent alkyne moiety (**2**).

Synthesis of AYC **1** commenced with 2-bromobenzylamine hydrochloride **3** (Chart 1). After *tert*-butoxycarbonyl (Boc) protection of **3** (98%), the resulting bromobenzene **4** was coupled with ethynylbenzene **5** under Sonogashira–Hagihara conditions<sup>32,33)</sup> to give **6** in good yield (90%).<sup>34)</sup> After removal of the Boc group with trifluoroacetic acid (TFA), amine **7** was converted to the corresponding thiourea **8** by

the action of phenyl isothiocyanate in refluxing acetone (69%).<sup>35)</sup> Desulfurization of **8** by treatment with methanesulfonyl chloride (MsCl) in the presence of triethylamine and 4-dimethylaminopyridine (DMAP)<sup>36)</sup> successfully furnished carbodiimide **1** (84%). As for AYC **2**, the synthesis was initiated with 2-aminobenzylalcohol **9**. Oxidation of alcohol **9** with MnO<sub>2</sub> into aldehyde, followed by addition of phenylethynyl magnesium bromide gave the secondary alcohol **10** (65% for two steps). Amine **10** was converted to the corresponding carbodiimide **2**, in an analogous sequence utilized in the synthesis of **1**, except for the additional step of tetrahydropyranyl (THP) ether formation. AYCs **1** and **2** were purified as rapidly as possible and stored at –20 °C to avoid decomposition.

With the desired AYCs in hand, the thermal CA reaction of **1** was carried out first (Chart 2). Although AYC **1** was heated at 110 °C for 72 h, the only product was urea **13** (19%), which might be generated through a slow hydrolysis of carbodiimide **1** by a trace amount of water contaminated in the reaction, with a recovery of most of the starting material **1**.

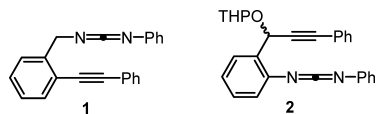
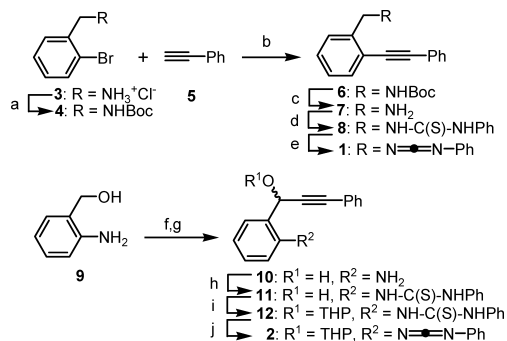


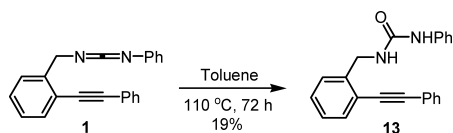
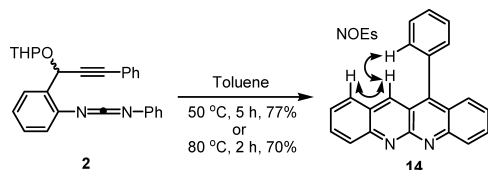
Fig. 1. Structures of Aryl–Yne–Carbodiimides **1** and **2**



Reagents and conditions: (a) Boc<sub>2</sub>O, NaHCO<sub>3</sub>, THF, H<sub>2</sub>O, rt, 4 h, 98%; (b) Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, CuI, Ph<sub>3</sub>P, Et<sub>3</sub>N, rt, 65 h; (c) TFA, benzene, rt, 2 h, then aq. NaHCO<sub>3</sub>, 89% (over 2 steps); (d) PhNCS, acetone, reflux, 24 h, 69%; (e) MsCl, Et<sub>3</sub>N, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, rt, 15 min, 84%; (f) MnO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C, 1 h; (g) PhC≡CMgBr, THF, 0 °C, 0.5 h, 65% (over 2 steps); (h) PhNCS, acetone, reflux, 24 h, 89%; (i) DHP, PPTS, CH<sub>2</sub>Cl<sub>2</sub>, 35 °C, 3 h, 96%; (j) MsCl, Et<sub>3</sub>N, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, rt, 15 min, 67%.

Chart 1

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Chart 2. Thermal Reaction of Aryl-Yne-Carbodiimide **1**Chart 3. Thermal Cyclization of Aryl-Yne-Carbodiimide **2**

Thus, we moved on to examining the CA reaction of AYC **2** (Chart 3).

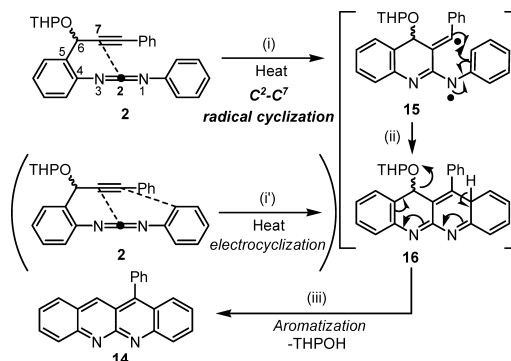
Notably, subjection of **2** to heating at 80 °C in toluene, without any reagents, resulted in the smooth and clean formation of **14** (70%), whose structure was unambiguously determined as a dibenzonaphthyridine derivative by  $^1\text{H}$ - $^1\text{H}$  COSY and NOE experiments. Moreover, the CA reaction of **2** proved to proceed even at 50 °C, in a retained yield (77%).<sup>37)</sup> Since conjugated AYCs tend to require higher temperature for their C<sup>2</sup>-C<sup>6</sup> thermal cyclizations,<sup>24–31)</sup> this result implied a possibility that C<sup>2</sup>-C<sup>7</sup> cyclization of nonconjugated AYCs proceeds more facily than that of conjugated ones.

Although the reaction mechanism for the thermal cyclizations of this class of compounds is still controversial,<sup>31)</sup> we tentatively envisaged that the C<sup>2</sup>-C<sup>7</sup> thermal cyclization of nonconjugated AYC **2** provided dibenzonaphthyridine derivative **14** as a result of the following three steps (Chart 4); (i) C<sup>2</sup>-C<sup>7</sup> conjunction between alkyne and carbodiimide moieties of **2** giving diradical species **15**, (ii) subsequent ring closure of **15** yielding tetracyclic closed-shell intermediate **16**, (iii) spontaneous elimination of alcohol (THPOH) at the benzylic position of **16** to render the aromaticity to the product (**14**). However, an alternative electrocyclic mechanism for the conversion of **2** to **16** (i') cannot be ruled out.

The reason why the CA reaction of **2** occurred much more smoothly than that of **1** is unclear, but one of the reasons is supposed to lie in the existence of the tetrahydropyranoxymethyl group at the benzylic position of **2**, which enables a smooth aromatization *via* the elimination of the corresponding alcohol.

Nonetheless, it is noteworthy that **14** is the first example of an azaaromatic compound prepared by reagent-free "C<sup>2</sup>-C<sup>7</sup>" thermal cyclization of "nonconjugated" AYCs, in contrast to the well-known "C<sup>2</sup>-C<sup>6</sup>" cyclization of "conjugated" AYCs.<sup>29–31)</sup> Moreover, compounds comprised of a dibenzo[*b,g*][1,8]naphthyridine system are reported to exhibit intriguing biological activities.<sup>21,22)</sup> Although a number of efficient synthetic methods for dibenzo[*b,g*][1,8]naphthyridines have been reported,<sup>38–41)</sup> the present method *via* the thermal isomerization of nonconjugated AYCs may alternatively be favored, because of the mildness of the conditions and the simple short-step procedure, which lead to a higher total yield of the product.

In conclusion, we have demonstrated that the thermal cycloaromatization of nonconjugated aryl-yne-carbodiimide **2** affords dibenzonaphthyridine **14**, while **1** was inert. Since the

Chart 4. Hypothetical Mechanisms for the Thermal Cyclization of Aryl-Yne-Carbodiimide **2**

thermal cyclization of **2** proceeded at mildly heated conditions (50 °C) in a reagent-free manner in good yield, the present route could potentially be a novel and useful synthetic methodology for benzonaphthyridine derivatives whose congeners are known to possess fascinating pharmacological properties. Further scope and limitation studies on thermal cyclization of nonconjugated aryl-yne-carbodiimides would be disclosed elsewhere.

## Experimental

**General** Anhydrous dichloromethane and tetrahydrofuran (THF) were purchased from Kanto Chemical Co., Inc. and used without further drying. Triethylamine was purchased from Nacalai Tesque Inc. and used as supplied. Other solvents were dried over activated molecular sieves 4A. All other chemicals were obtained from local vendors, and used as supplied unless otherwise stated. Analytical thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F<sub>254</sub> pre-coated plates (0.25-mm thickness). For column chromatography, silica gel 60 (70–270 mesh ASTM, Merck), or aluminum oxide 90 (Merck) were used. IR spectra were recorded on a Shimadzu FT-IR-8300. NMR spectra were recorded on a JEOL JNM-LA400 (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with reference to internal residual solvent [ $^1\text{H}$ -NMR,  $\text{CHCl}_3$  (7.26),  $\text{CHD}_2\text{OD}$  (4.78);  $^{13}\text{C}$ -NMR,  $\text{CDCl}_3$  (77.0)]. The following abbreviations are used to designate the multiplicities: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet. Mass spectra were recorded on a JEOL JMS600 under FAB conditions using *m*-nitrobenzyl alcohol (NBA) as a matrix.

**Synthesis of Carbodiimide 1** Carbamate (**4**): A solution of 2-bromobenzyl amine hydrochloride **3** (1.11 g, 5.00 mmol),  $\text{NaHCO}_3$  (1.26 g, 15.0 mmol), di-*t*-butyl dicarbonate (1.31 g, 6.00 mmol) in wet THF (THF–water=10 ml:10 ml) was stirred at room temperature for 4 h. The resulting mixture was neutralized with 1 N HCl, and extracted with EtOAc. The combined organic layer was washed with brine, dried over  $\text{MgSO}_4$  and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane–EtOAc) to give carbamate **4** (1.40 g, 98%) as a colorless oil.  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 1.45 (9H, s), 4.38 (2H, s), 5.07 (1H, s), 7.13 (1H, ddd,  $J=7.8, 7.3, 1.7$  Hz), 7.29 (1H, ddd,  $J=7.3, 7.3, 1.0$  Hz), 7.37 (1H, dd,  $J=7.3, 1.7$  Hz), 7.54 (1H, dd,  $J=7.8, 1.0$  Hz).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$ : 27.3, 28.3, 44.8, 79.6, 85.1, 123.4, 127.6, 128.9, 130.0, 132.7, 146.7, 155.8.

**Amine (7):** Under argon atmosphere, to a solution of **4** (1.43 g, 5.00 mmol) and ethynylbenzene (1.37 ml, 12.5 mmol) in triethylamine (40 ml) was added bis(triphenylphosphine)palladium(II) dichloride (175 mg, 0.250 mmol), copper(I) iodide (47.6 mg, 0.250 mmol), and triphenylphosphine (131 mg, 0.500 mmol) at room temperature. After being stirred at room temperature for 65 h, the mixture was neutralized with 2 N HCl, diluted with EtOAc, filtered through a pad of celite, and the filtrate was washed with brine, dried over  $\text{MgSO}_4$ , and the solvent was removed *in vacuo*. The residue was roughly purified by alumina column chromatography (hexane–EtOAc) to give phenyl ethynyl benzene **6** (1.39 g), which was used in the next reaction without further purification.

To a solution of the above crude ethynyl benzene **6** in benzene (40 ml) was added trifluoroacetic acid (7 ml), and the mixture was stirred at room temperature for 2 h. The resulting mixture was neutralized with saturated aq.  $\text{NaHCO}_3$  and extracted with EtOAc. The combined organic layer was

washed with brine, dried over  $\text{MgSO}_4$ , and evaporated *in vacuo*. The residue was purified by alumina column chromatography (EtOAc) to give amine **7** (930 mg, 89% for two steps), as a colorless solid.  $^1\text{H-NMR}$  ( $\text{CD}_3\text{OD}$ )  $\delta$ : 4.38 (2H, s), 7.40—7.43 (3H, m), 7.45—7.54 (3H, m), 7.57—7.67 (3H, m).

Thiourea (**8**): Under argon atmosphere, to a solution of amine **7** (440 mg, 2.12 mmol) in acetone (5 ml) was added dropwise phenyl isothiocyanate (0.25 ml, 2.1 mmol) at room temperature. After being stirred under reflux for 24 h, the reaction mixture was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography (hexane–EtOAc) to give thiourea **8** (501 mg, 69%) as a colorless solid.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 5.04 (2H, s), 6.78 (1H, s), 7.06 (1H, ddd,  $J=7.8, 7.8, 1.0$  Hz), 7.13—7.20 (4H, m), 7.23—7.31 (5H, m), 7.35—7.37 (2H, m), 7.45 (1H, dd,  $J=7.3, 1.0$  Hz), 7.50 (1H, dd,  $J=7.3, 1.0$  Hz), 8.77 (1H, s).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 47.9, 86.8, 97.4, 122.2, 122.3, 124.7, 127.6, 128.2, 128.4, 128.5, 129.0, 129.8, 131.4, 132.1, 135.9, 138.8, 180.0. FAB-MS  $m/z$ : 343 ( $\text{M}+\text{H}$ ) $^+$ .

Carbodiimide (**1**): At 0 °C under argon atmosphere, to a solution of thiourea **8** (241 mg, 0.704 mmol), triethylamine (0.30 ml, 2.1 mmol), and 4-dimethylamino pyridine (DMAP, 3 mg, 0.03 mmol) in dichloromethane (7 ml) was added dropwise methanesulfonyl chloride (0.11 ml, 1.4 mmol). After being stirred for 15 min at 0 °C, the mixture was filtered through a pad of silica gel and the filtrate was concentrated *in vacuo*. The residue was purified by alumina column chromatography (hexane–EtOAc) to give carbodiimide **1** (182 mg, 84%) as a colorless solid.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 4.78 (2H, s), 6.99—7.04 (3H, m), 7.16 (2H, dd,  $J=7.3, 1.0$  Hz), 7.25—7.35 (5H, m), 7.46—7.55 (4H, m).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 49.1, 86.5, 94.5, 121.9, 122.7, 123.7, 124.7, 127.7, 127.8, 128.2, 128.4, 128.7, 129.1, 131.5, 132.2, 137.1, 139.2, 139.8. IR ( $\text{CHCl}_3$ )  $\text{cm}^{-1}$ : 2103. FAB-MS  $m/z$ : 309 ( $\text{M}+\text{H}$ ) $^+$ .

**Synthesis of Carbodiimide 2** Alcohol (**10**): To a solution of 2-aminobenzylalcohol **9** (1.80 g, 15.0 mmol) in dichloromethane (75 ml) was added manganese(II) oxide (16 g, 0.59 mmol) at 0 °C. After being stirred vigorously at 0 °C for 1 h, the suspension was filtered, and the filtrate was concentrated *in vacuo* to give the corresponding aldehyde. On the other hand, in another apparatus, under argon atmosphere, to a solution of ethynyl benzene (4.1 ml, 38 mmol) in THF (100 ml) was added ethyl magnesium bromide (1 M in THF, 33 ml, 33 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h to give phenylethynyl magnesium bromide solution. At 0 °C, under argon atmosphere, to the above solution of Grignard reagent was added dropwise the solution of aldehyde in THF (100 ml). After being stirred at 0 °C for 30 min, the reaction was quenched with saturated aq.  $\text{NH}_4\text{Cl}$  and diluted with EtOAc. The organic layer was separated, washed with brine, dried over  $\text{MgSO}_4$ , and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane–EtOAc) to give alcohol **10** (2.2 g, 65%) as a colorless solid.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 2.57 (1H, brs), 4.27 (2H, brs), 5.71 (1H, s), 6.14 (1H, dd,  $J=8.0, 1.2$  Hz), 6.80 (1H, ddd,  $J=8.0, 7.6, 1.2$  Hz), 7.17 (1H, ddd,  $J=8.0, 7.6, 1.2$  Hz), 7.32—7.34 (3H, m), 7.49—7.51 (3H, m).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 63.9, 87.3, 87.4, 116.9, 118.5, 122.3, 124.6, 128.0, 128.3, 129.7, 131.8, 145.1. IR ( $\text{CHCl}_3$ )  $\text{cm}^{-1}$ : 3580, 3390, 2190. FAB-MS  $m/z$ : 233 ( $\text{M}^+$ ), 206 ( $\text{M}-\text{OH}$ ) $^+$ .

Thiourea (**11**): Thiourea **11** was prepared from amine **10** (223 mg, 1.00 mmol) in 89% yield by a procedure similar to that employed for compound **8**.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 3.70 (1H, s), 5.73 (1H, s), 7.18 (1H, ddd,  $J=7.5, 7.1, 1.0$  Hz), 7.22—7.34 (8H, m), 7.35 (1H, ddd,  $J=8.1, 7.8, 1.5$  Hz), 7.40 (2H, ddd,  $J=8.1, 7.8, 1.2$  Hz), 7.62 (1H, dd,  $J=8.1, 1.5$  Hz), 7.65 (1H, dd,  $J=7.8, 1.5$  Hz), 8.50 (1H, s), 8.56 (1H, s).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 62.1, 86.6, 87.3, 121.8, 125.0, 126.7, 127.0, 127.8, 128.0, 128.3, 128.7, 129.2, 131.6, 135.1, 136.0, 136.3, 180.0. IR ( $\text{CHCl}_3$ )  $\text{cm}^{-1}$ : 3274, 2231, 1539. FAB-MS  $m/z$ : 359 ( $\text{M}+\text{H}$ ) $^+$ , 341 ( $\text{M}-\text{OH}$ ) $^+$ .

Tetrahydropyranyl Ether (**12**): To a solution of alcohol **11** (348 mg, 0.970 mmol) in dichloromethane (10 ml) was added 3,4-dihydro-2H-pyran (DHP, 0.26 ml, 2.9 mmol), pyridinium *p*-toluenesulfonate (PPTS, 24 mg, 0.10 mmol) at 0 °C. After being stirred at 35 °C for 3 h, the reaction was quenched with saturated aq.  $\text{NaHCO}_3$  and diluted with chloroform. The organic layer was separated, washed with brine, dried over  $\text{MgSO}_4$  and evaporated *in vacuo*. The residue was purified by silica gel column chromatography (hexane–EtOAc) to give tetrahydropyranyl ether **12** (412 mg, 96%) as a colorless solid.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.26—1.83 (6H, m), 3.49 (1H, m), 3.73 (1/2H, m), 3.90 (1/2H, m), 4.44 (1/2H, m), 4.94 (1/2H, m), 5.65 (1/2H, s), 5.73 (1/2H, s), 7.16—7.40 (10H, m), 7.51 (1H, ddd,  $J=7.6, 5.6, 1.2$  Hz), 7.55 (1H, ddd,  $J=7.8, 5.6, 1.2$  Hz), 7.60 (1H, dd,  $J=7.6, 1.0$  Hz), 7.84 (1/2H, dd,  $J=7.8, 1.0$  Hz), 7.88 (1/2H, dd,  $J=7.8, 1.0$  Hz), 8.61 (1/2H, s), 8.67 (1/2H, s), 8.85 (1H, s).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 18.7, 19.6, 24.8, 25.0, 25.2, 29.8, 30.0, 30.5, 61.9, 62.7, 63.2, 66.0, 84.8, 86.0, 86.4, 87.6, 94.4, 95.1, 96.5, 121.9, 122.1, 124.3, 125.4, 126.2, 126.9, 127.8, 128.0, 128.1, 128.3, 128.4, 128.6, 128.7, 128.8, 129.1, 129.3, 129.5, 132.0, 136.4, 137.0,

137.1, 179.9, 180.0. IR ( $\text{CHCl}_3$ )  $\text{cm}^{-1}$ : 3302, 3150, 2225, 1510. FAB-MS  $m/z$ : 443 ( $\text{M}+\text{H}$ ) $^+$ .

Carbodiimide (**2**): Carbodiimide **2** was prepared from **12** (315 mg, 0.711 mmol) in 67% yield, by a procedure similar to that employed for compound **1**.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.26—1.83 (6H, m), 3.60 (1H, m), 3.94 (1/2H, t,  $J=7.8$  Hz), 4.13 (1/2H, t,  $J=7.8$  Hz), 4.78 (1/2H, m), 5.33 (1/2H, m), 6.12 (1/2H, s), 6.17 (1/2H, s), 7.14—7.29 (11H, m), 7.44 (1H, ddd,  $J=7.6, 6.7, 1.0$  Hz), 7.45 (1H, dd,  $J=6.7, 1.0$  Hz), 7.74 (1/2H, dd,  $J=7.6, 1.0$  Hz), 7.82 (1/2H, dd,  $J=7.6, 1.0$  Hz).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 18.8, 19.1, 25.1, 25.3, 30.2, 30.7, 61.8, 62.0, 63.0, 64.2, 67.9, 71.6, 85.8, 86.6, 86.8, 87.9, 95.3, 96.8, 122.6, 122.8, 122.9, 124.2, 125.0, 125.4, 125.5, 125.9, 128.1, 128.1, 128.2, 128.3, 128.5, 128.7, 129.1, 129.2, 129.3, 129.4, 130.0, 130.5, 130.9, 131.8, 131.8, 136.0, 136.5, 138.1, 138.3. IR ( $\text{CHCl}_3$ )  $\text{cm}^{-1}$ : 2248, 2144. FAB-MS  $m/z$ : 409 ( $\text{M}+\text{H}$ ) $^+$ .

**Thermal Cycloaromatization of Carbodiimide 2** 11-Phenyl-dibenzo[*b,g*][1,8]naphthyridine (**14**): A solution of carbodiimide **2** (87 mg, 0.21 mmol) in toluene (5 ml) was stirred at 50 °C for 5 h under argon atmosphere. After being cooled to room temperature, the reaction solution was concentrated under reduced pressure. The residue was purified by alumina column chromatography (hexane–EtOAc) to give benzonaphthyridine derivative **14** (67 mg, 77%) as a red solid.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 7.41 (1H, ddd,  $J=8.8, 6.6, 1.1$  Hz), 7.46 (1H, ddd,  $J=8.5, 6.6, 0.7$  Hz), 7.53—7.56 (2H, m), 7.69—7.70 (3H, m), 7.75 (1H, dd,  $J=8.8, 1.1$  Hz), 7.80 (1H, ddd,  $J=8.8, 6.6, 1.1$  Hz), 7.81 (1H, ddd,  $J=9.2, 6.6, 1.1$  Hz), 7.86 (1H, dd,  $J=8.5, 1.1$  Hz), 8.35 (1H, dd,  $J=9.2, 0.7$  Hz), 8.39 (1H, dd,  $J=8.8, 1.1$  Hz), 8.77 (1H, s).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 119.1, 124.7, 125.8, 125.9, 126.4, 126.8, 128.5, 128.7, 128.9, 130.0, 130.5, 130.7, 131.6, 132.0, 135.2, 137.7, 149.9, 152.7, 152.9, 152.9. IR ( $\text{CHCl}_3$ )  $\text{cm}^{-1}$ : 1580. UV  $\lambda_{\text{max}}$  ( $\text{CH}_2\text{Cl}_2$ ) nm (log  $\epsilon$ ): 275 (5.46). FAB-MS  $m/z$ : 307 ( $\text{M}+\text{H}$ ) $^+$ .

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## References and Notes

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